Example 45

**[0518]** Bovine Serum Albumin (0.1 g) was dissolved in DI water (4 mL) and 100 colony forming units of Escherichia coli were spiked into the solution. The solution was atomized and collected with a stainless steel vessel containing a volume greater than $V_0$ of a second liquid with no known sterilizing properties. After primary desiccation, particles were collected, washed, and vacuum dried. The particles were then placed in foil pouches and transferred to a 750 mL steel autoclave equipped with an inlet and outlet valve, pressure gauge, and safety valve. The autoclave was filled with $scCO_2$ (300 g liquid $CO_2$) and transferred to the supercritical (sc) state by heating the autoclave (38° C., 8.5 MPa). Particles were subjected to $scCO_2$ treatment for around 30 minutes before depressurization of the autoclave and collection of the sterile powder. After dissolution of 10 mg of powder in 1 mL of deionized water, 1 mL of the dissolved powder was incubated in Fluid Thioglycollate Medium for a period of 14 days to ensure no microbial growth.

Example 46

**[0519]** A solution of protein (20 mg/mL) was prepared in deionized water. The surface tension (air-water) of this solution was measured using a Kruss K11 tensiometer fitted with a Wilhelmy plate. The surface tension was recorded until equilibrium was reached. The solution exhibited a decrease of approximately 10 mN/m as compared to neat deionized water. This demonstrated the ability of the surfactant to act as a surfactant (FIG. **13**).

Example 47

**[0520]** A first solution of human IgG (first liquid A) was prepared by reconstituting human IgG powder in deionized water to a protein concentration of approximately 50 mg/mL. The solution was desalted. A second solution of human IgG (first liquid B) was prepared by reconstituting human IgG powder in deionized water to a protein concentration of approximately 50 mg/mL. The solution was desalted and a quantity of a plasticizer (5 mg/mL) was added. The solutions were separately atomized and collected with stainless steel vessels containing volumes greater than $V_0$ of a second liquid held under conditions of gentle stirring. In both cases, the temperature of the first liquid and the second liquid during the particle formation process was kept above the glass transition temperature of the plasticizer excipient in first liquid B. In both cases, these resulted in a Peclet number of greater than 1 for the human IgG in the first liquid. After primary desiccation, particles were collected, washed, and vacuum dried to remove residual liquid. SEM images revealed identifiable particulate matter and indicated that the plasticizer afforded control over the particle morphology. First liquid A was associated with particles comprising an internal void space and wrinkled surfaces. First liquid B was associated with particles comprising lesser degrees of internal void spaces and wrinkled surfaces.

Example 48

**[0521]** A first solution of human IgG (first liquid A) was prepared by reconstituting human IgG powder in deionized water to a protein concentration of approximately 50 mg/mL. The solution was desalted. A second solution of human IgG (first liquid B) was prepared by reconstituting human IgG powder in deionized water to a protein concentration of approximately 50 mg/mL. The solution was desalted and a quantity of a surfactant (2 mg/mL) was added. The solutions were separately atomized and collected with stainless steel vessels containing volumes greater than $V_0$ of a second liquid held under conditions of gentle stirring. In both cases, the temperature of the first liquid and the second liquid during the particle formation process was kept above the glass transition temperature of the surfactant excipient in first liquid B. In both cases, this resulted in a Peclet number of greater than 1 for the human IgG in the first liquid. After primary desiccation, particles were collected, washed, and vacuum dried to remove residual liquid. SEM images revealed identifiable particulate matter and indicated that the surfactant afforded control over the particle morphology. First liquid A was associated with particles comprising an internal void space and wrinkled surfaces. First liquid B was associated with particles comprising lesser degrees of internal void spaces and wrinkled surfaces. This may have to do with the surfactant effectively plasticizing the drop and the particle during the particle formation process, in addition to mitigating forces at the interface between the second liquid and the drop/particle. A sample of the particles produced from first liquid A were suspended in a non-aqueous medium in such a way that the average concentration of human IgG in the formulation was approximately 400 mg/mL (sample A). A sample of the particles produced from first liquid B were suspended in a separate volume of the same non-aqueous medium such that the average concentration of human IgG in the formulation was approximately 400 mg/mL (sample B). A sample for comparison was produced by reconstituting human IgG powder in deionized water to a protein concentration of approximately 400 mg/mL (sample C). The inherent viscosities of the non-aqueous medium and the deionized water (no protein load) were approximately 6 mPa·s and 1 mPa·s, respectively. The viscosities of all three samples were tested using a rheometer. In terms of increasing viscosity, the results indicated that sample B<sample A<sample C, i.e., that the particles from first liquid B provided the lowest formulation viscosity at the concentration of interest. This may be a byproduct of their smoother, more spherical morphology.

Example 49

**[0522]** Human IgG powder was reconstituted in deionized water to a protein concentration of approximately 24 mg/mL. The solution was desalted, after which it was atomized and collected with a stainless steel vessel containing a volume greater than $V_0$ of butyl acetate held near room temperature under conditions of gentle stirring. After primary desiccation, particles were collected, washed, and vacuum dried to remove residual liquid. HIM images revealed identifiable particulate matter. Cross-sections of the particles indicated an absence of pores (substantially free from any internal void spaces) and a correspondingly low particle porosity (FIGS. **14**A-**14**B) as compared to the particles of FIG. **3**A. The particles were found to have a circularity of 0.900 and a roughness of 2.342 as compared to the particles of FIG. **3**A.

Discussion

**[0523]** As demonstrated in the exemplary material, particle morphology was manipulated variously and exten-